

Chordoma of the thoracic vertebrae in a Bengal tiger (*Panthera tigris tigris*)

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ABSTRACT: A 19-year-old female Bengal tiger (*Panthera tigris tigris*) was presented with hind limb weakness, ataxia and respiratory distress. Computed tomography revealed a mass between the left side of the T7 vertebra and the base of the left 7th rib. The tiger then died, and necropsy was performed. Grossly, the vertebral mass was 6 × 5.7 × 3 cm, and invaded the adjacent vertebral bone and compressed the T7 spinal cord. Histologically, the mass was composed of large, clear, vacuolated and polygonal cells with osteochondral matrix. Cellular and nuclear atypia were moderate. The vacuolated cells stained positively for cytokeratin and vimentin and negatively for S-100. Based on these findings, the present case was diagnosed as a vertebral chordoma; the first report in a tiger.

KEY WORDS: chordoma, neurological symptom, tiger, vertebral tumor

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Chordoma is a rare tumor of notochordal remnants origin and most commonly occurs in ferrets. In ferrets, chordoma usually occurs at the tip of their tail. In humans, dogs, cats, rats and minks, chordoma develops mainly in the sacrococcygeal region [8, 9]. The histologic hallmark of chordoma is large, clear and vacuolated cells (physaliferous cells) that show immunoreactivity to cytokeratin and vimentin [7]. Chordomas of the paraspinal region are rare; those arising from the cervical vertebrae are reported in ferrets [16], dogs [6, 16, 17] and cats [4, 5], from the intervertebral disc space in a dog [12] and from the lumbosacral vertebrae in rats [13, 14]. Here, we describe a case of thoracic vertebral chordoma in a tiger with spinal cord symptoms.

A 19-year-old female Bengal tiger (*Panthera tigris tigris*) kept in a zoo was presented with hind limb weakness, subsequent hind limb ataxia and respiratory distress for 2 months. Computed tomography examination revealed a mass located between the left side of the vertebral body and left rib at the T7–T8 level. The tiger suddenly died after the examination, and necropsy was performed. At necropsy, a whitish mass, 6 × 5.7 × 3 cm in size, was observed between the left side of the T7 vertebra and the base of the left 7th rib, extending into the T7–T8 intercostal muscle (Figs. 1 and 2). The mass invaded the adjacent bone tissue (vertebral body, arch and transverse process), extended along the left T7 nerve root and protruded into the spinal canal (Supplementary Fig. 1). The mass, lungs, heart, liver, spleen, intestines, kidneys,

pancreas, ovaries and uterus were removed and examined.

The tissues were fixed in 10% neutral-buffered formalin and embedded in paraffin. Histologic sections cut at 4 μm were stained with hematoxylin and eosin (HE). Immunohistochemical analyses were performed using monoclonal antibodies against cytokeratin (clone AE1/AE3, 1:1,000; Dako, Glostrup, Denmark), vimentin (clone V9, ready to use; Dako) and polyclonal antibody against S-100 (ready to use; Dako). After dewax, sections for immunohistochemistry against cytokeratin and vimentin were pretreated by microwave for 20 min in 0.01 M citrate buffer (pH 6.0) for antigen retrieval. Sections were incubated with 3% H₂O₂ in phosphate-buffered saline (PBS) for 10 min to quench endogenous peroxidase. Thereafter, the sections were treated with 5% skimmed milk in PBS for 30 min and incubated with each primary antibody for 1 hr at room temperature, followed by 1 hr incubation with peroxidase-conjugated secondary antibody (Histofine Simple Stain MAX PO; Nichirei, Tokyo, Japan). Positive reactions were detected with 3, 3'-diaminobenzidine (DAB Substrate Kit; Nichirei). Sections were counterstained lightly with hematoxylin.

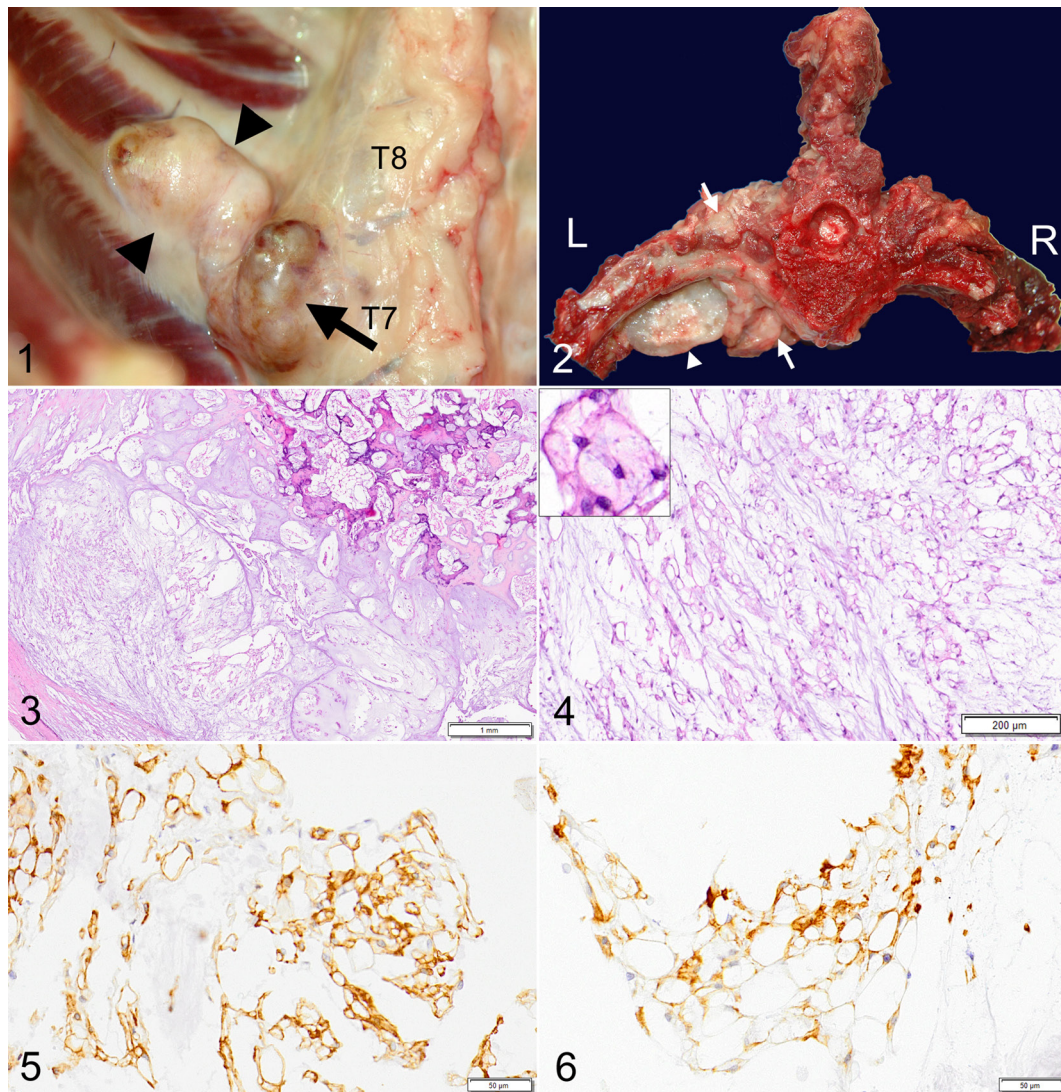
Microscopically, the mass was composed of a mixture of hypocellular myxoid areas, bone and cartilaginous tissues (Fig. 3). Neoplastic cells were arranged in cords, nests and small islands (Fig. 4), and had large, clear and vacuolated cytoplasm with round to oval nuclei (Fig. 4, inset). Immunohistochemically, the vacuolated cells were positive for cytokeratin AE1/AE3 and vimentin (Figs. 5 and 6, respectively). There was no immunoreactivity for S-100. In the T7 to T8 spinal cord, vacuolation of the white matter, swollen axons (spheroids), infiltration of foamy macrophages and activated astrocytes (gemistocytes) were observed (Supplementary Fig. 2). In other organs, chronic nephropathy and pulmonary atelectasis were observed. No metastasis was found.

Based on these findings, this case was diagnosed as chordoma arising from the thoracic vertebrae. Chondroma,

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chondrosarcoma, myxosarcoma and liposarcoma should be considered in the differential diagnosis [14]. Chordoma is primarily composed of large, clear and vacuolated (physaliferous) cells which stain immunohistochemically for cytokeratin and vimentin [9]. The cytokeratin immunoreactivity can be a diagnostic criterion, since the mesenchymal tumors described above do not stain for cytokeratin [7, 9]. S-100 is

not a good marker; some chordomas as well as cartilage and adipose tumors stain positively for the marker [4].

In humans, chordoma is classified as classical chordoma, chondroid chordoma and dedifferentiated (sarcomatoid) chordoma [10]. The present case can be classified as classical chordoma, since the main component was physaliferous cells. There are some reports of chondroid chordoma, a

- Fig. 1. The mass between the left side of vertebra and the base of the T7 rib (arrow), extending into the T7-8 intercostal muscle (arrowheads).
 Fig. 2. Transverse image of the T8 vertebra. The mass is located between the left side of the T7-8 vertebral bone and left rib (arrows), extending into the T7-8 intercostal muscle (arrowhead).
 Fig. 3. The mass is composed of large, clear and vacuolated cells admixed with osteochondral matrix. HE stain. Bar: 1 mm.
 Fig. 4. The neoplastic cells are arranged in cords, nests and small islands, and have large, clear and vacuolated cytoplasm (inset). HE stain. Bar: 200 μm .
 Fig. 5. The vacuolated cells show positive reaction for cytokeratin AE1/AE3. DAB chromogen, counterstained with hematoxylin. Bar: 50 μm .
 Fig. 6. The vacuolated cells show positive reaction for vimentin. DAB chromogen, counterstained with hematoxylin. Bar: 50 μm .

variant with chondromatous component in dogs [16, 18] and a cat [4].

Depending on the location, chordoma can involve the nervous system. Compression of the adjacent spinal cord can cause neurological symptoms, such as paralysis, ataxia, loss of proprioception [17], urinary incontinence and constipation [12]. In the present case, the hind limb weakness is probably attributable to the compression of the thoracic (T7–T8) spinal cord. In human patients with vertebral chordoma, pain and autonomic dysfunction are the clinical signs [19]. Besides, some cases are reported to metastasise to the lungs, bone, soft tissue, liver, lymph nodes and skin [2]. In animals, metastasis to the skin is reported in ferrets [11, 17], to the retropharyngeal lymph nodes in a cat [5] and to the lungs in F344 rats [3]. Therefore, some chordomas can exhibit malignant behavior. In this case, the tumor invaded the surrounding vertebral bone with osteolysis and compressed the spinal cord with degeneration of axons and myelin, suggesting a malignant.

In tigers, more than ten tumors are reported to date. However, tumors of the nerves systems are only 2 cases; an intracranial meningioma [1] and a cutaneous peripheral nerve sheath tumor [15]. Chordoma is uncommon tumor in zoo and wildlife animals. However, it should be considered in the differential diagnosis when mass is present in the thoracic vertebrae with neurological symptoms. The present case is the first report of chordoma in a tiger. Further cases are required to understand the clinical behavior of vertebral chordoma.

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